α - THALASSAEMIA PREVALENCE AND PATTERN IN NORTHERN PAKISTAN

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Zuhur-ur-Rehman, M. Saleem, A. A. Alvi, M. Anwar, P. A. Ahmed, M. Ahmad (Haematology Department, Armed Forces Institute of Pathology, Rawalpindi.)

ABSTRACT

The level of Hb Bart's is directly related to the inheritance of cc-thalassaemia gene. Hb electrophoresis for Hb Bait's in the cord blood is a very simple method of finding out the prevalence of oc-thalassaemia gene in a given population. A study was, therefore, carried out to find out the prevalence of cc- thalassaemia gene in the population of northern Pakistan by estimating the concentration of Hb Bait's in 500 cord blood samples during the period 1986-87 at AFIP Rawalpindi. Hb Bait's was detected in 12 neonates, thus indicating a rate of 2.4% of general population as carrier of cc-thalassaemia gene. Two distinct groups were recognized. The first group was composed of 9 (75%) neonates, in which Hb Bait's levels varied between 2.0% to 3.5%, while the second group of 3 neonates (25%) showed a level of 5.8% to 6.3%. The former group was considered to be carrying x-thalassaemia-2 gene and the latter group as carrier of oc-thalassaemia-1 gene. Neither Hb H disease nor Hb Bait's hydrops foetalis syndrome was detected in this series (JPMA 41:246, 1991).

INTRODUCTION

Thalassaemias are a heterogeneous group of inherited disorders, characterised by deficient/absent synthesis of globin part of the Hb molecule resulting into various clinical syndrome[1]. Depending upon the type of chain affected the thalassaemias are classified into alpha, beta, gamma or delta thalassaemias. The cc -thalassaemia syndromes are characterised by absent or non-functioning of normal α -globin genes, thus resulting in an imbalance of α -globin chain synthesis. In majority of cases it occurs as a consequence of gene deletion[2]. In normal individuals alpha chains are synthesised under the control of 4 alpha globin genes, located on chromosome 162 The normal genotype is expressed as (α α / α α). α - thalassaemia is characterized by four subtypes. In cc - thalassaemia-2 there is absence of one cc -globin gene (—α / α α), while in cc -thalassaemia-1 there is loss of 2 genes, either from the same pair of chromosomes (— —/ α α) or one gene each from both the chromosomes (—α /— α). These two forms constitute α -thalassaemia carrier states. Hb H disease, a compound heterozygous state with only one functional gene (— -/- α), is an important clinical entity. Hb Bart's hydrops foetalis syndrome results from deletion of all the four alpha globin genes (--/--) and is incompatible with life[3]. The α - thalassaemia in neonates is characterized by decreased synthesis of chains resulting into ac-cumulation of excessive free gamma chains in the form of tetramers (r4), called Hb Bart's. The level of Hb Bart's in cord blood is directly related to the number of cc -thalassaemia genes deficient in that individual 2 In a normal neonate, the level of Hb Bart's is very low (upto 0.2 to 0.5%)[4]. The level of Hb Bart's is below 3% in α -thalassaemia-2, while in α - thalassaemia-1, it ranges between 3. 5-&5%. Hb H disease is characterized by Hb Bart's levels of between 20-25%, whereas in Hb Bart's hydrops foetalis syndrome, the concentration of Hb Bart's, is between 80% to 90%[5]. In infants Hb Bart's disappears at the age of six months and for detection of carrier states in adults the available methods are relatively expensive and cumbersome. The estimation of Hb Bart's in cord blood is, therefore, an easy, sensitive, cheap and reliable method for the detection of α -thalassaemia in early life[6]. The α -thalassaemia gene has been found to be prevalent throughout the world[3]. It is highest amongst the

countries in South East Asia[7], Mediterranean region[8] and in people of Black ancestory[9]. So far, screening of α -thalassaemia gene has not been carried out extensively in Pakistan. Therefore, the present study has been undertaken with a view to find out the overall prevalence, various patterns and detection of probable genotype in the population of northern Pakistan by screening the neonates for Hb-Bart's.

MATERIALS AND METHODS

Consecutive cord blood samples of 500 neonates were collected from local military hospital of Rawalpindi. EDTA was used as anticoagulant. After collection, the specimens were refregirated immediately and transported to AFIP Rawalpindi without delay. Majority of neonates belonged to northern Pakistan. Name, sex, place of origin, caste, and other relevant findings were recorded in a proforma. Red cells lysates were prepared by standard method and were subjected to electrophoresis on cellulose acetate strip at alkaline pH (8.1) using tris-EDTA-borate as buffer. On visual inspection Hb Bart's was detected as a fast moving haemoglobin towards anode, ahead of Hb A and Hb F. The strip was stained with 0.2% Ponceau S stain after fixing it in 3% trichloracetic acid. Hb Bart's was quantitated by elution from cellulose acetate strip and its concentration was measured by photometry.

RESULTS

Twelve cord blood samples revealed visible band of Hb Bart's. Data pertaining to these neonates showing Hb Bart's is summarized in Table.

TABLE. Summary of Hb Bart's cases.

S.No.	Sex	Place	Caste	Hb Bart's	Type of ∝-Thalassaemia
1.	M	Abbottabad	Syed	2.0% \	
2.	F	Islamabad	Pathan	2.2% :	
3.	M	Rawalpindi	Satti	2.3% :	
4.	F	Rawalpindi	Arain	2.6% :	
5.	M	Poonch	Sudhan	2.8% :	∝ — thalassaemia-2
6.	F	Rawalpindi	Gujar	2.8% :	
7.	M	Gujrat	Syed	2.9% :	
8.	F	Rawalpindi	Syed	3.4% :	
9.	M	Nawabshah	Arain	3.5% /	
10.	F	Rawalpindi	Rajput	5.8% \	
11.	F	Sialkot	Mughal	5.8% :	∝-thalassaemia-1
12.	F	Rawalpindi	Rajput	6.3% /	

On the basis of detectable levels of Hb Bart's an overall prevalence of α -thalassaemia gene has been found to be 2.4%. The levels of Hb Bart's varied from 2.0 to 6.30% and there were two modes of distribution. One group in which Hb Bart's ranged from 2.0 to 3.5%, included 9(75%) neonates. The other group consisted of only 3 (25%) neonates with Hb Bart's ranging from 5.8% to 6.3%. The former group was considered to be carrying α -thalassaemia-2 gene and the latter α -thalassaemia-1 gene. No Hb H disease or Hb Bart's hydrops foetalis syndrome was detected in this study.

DISCUSSION

Ml populations of the world carry α -thalassaemia gene. Its prevalence varies from 1% to over 80%[3] α -thalassaemia gene with full spectrum of clinical presentations is widely distributed in South East Asia[7]. The populations residing in Mediterranean region, have been found suffering from both classical pattern and non deletion type of disease[4]. Another group comprised of Blacks has mild α -thalassaemia but frequency is upto 27%. In this group Hb H-disease is rare and Hb Bart's hydrops foetalis is not on record[9]. In Asia the area starting from western border of Burma and extending upto Turkey presents a pattern of α -thalassaemia similar to that found in Blacks. The carriers of α -thalassaemia are common, but Hb H-disease is rare and Hb Bart's hydrops foetalis syndrome is not found. In some areas of southern India 50% of the population is carrying cc -thalassaemia representing areas of focal concentrations of this gene[10]. 50% of people residing in the eastern coast of Saudi Arabia also possess α -thalassaemia gene[11] α -thalassaemia has been studied to a very small extent in Indo-Pak subcontinent. Chouhan et al[12] studied α -thalassaemia in India and pointed out a prevalence of 2.05%. Vora and colleagues[13] found the prevalence in Indian people as 0.45% only. In another study in Indian state of Orrissa a frequency of 0.29% was recorded[6]. The only study of some value conducted in Pakistan revealed a prevalence of 0.94% in population in and around Lahore[14]. In the present study conducted at AFIP, 2.40% of population of northern Pakistan has been found to be carrying α -thalassaemia gene. All the castes of the region are equally affected except Syeds in whom the prevalence seems to be high. It can be attributed to the closer inter-marriages in this particular group. No focal concentration of the abnormal gene was found in the population of northern Pakistan in this study. As a result of this study, 9 neonates were found as carriers of cc -thalassaemia-2 gene whereas, only 3 neonates were suffering from α -thalassaemia- 1. No case of Hb H disease or Hb Bart's hydrops foetalis syndrome was detected during this study. The absence of Hb H disease and Hb Bart's hydrops foetalis in our population is probably indicative of the presence of a genotype different from that of classical α -thalassaemia found in South East Asia and Mediterranean region. In the latter case the 2 alpha genes are deleted from the same chromosome (—. —f α α) i.e. cis position, whereas Blacks have been found to be carrying α -thalassaemia-1 gene deletion in transposition (—α /— α)[9], In India, gene mapping studies in α - thalassaemia- 1 revealed two genes deletion in transposition (—α /— α)6. On the basis of the rarity of Hb H disease and absence of Hb Bart's hydrops foetalis syndrome and its similarities to α -thalassaemia presentation and Indians, it is likely that our population also carries similar genotype i.e., (—α /— α). This needs confirmation by conducting gene mapping studies in our population. This study has revealed that cc -thalassaemia trait is present in 2.4% of the population of northern Pakistan. It is further concluded that severe forms of α -thalassaemia i.e., Hb H-disease and FIb Bart's hydrops foetalis syndrome have not been detected in this study. The most likely genotype is (—α /— α) trans and not (— —f α α) cis. which precludes severe form of disease.

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